REMARKS

Claims 1, 2, 4-10, and 12-15 are pending in the present application. Claim 1 has been amended, support for which can be found at, for example, page 83, lines 1 to 8 of the specification. No new matter has been added. Upon entry of the present amendment, claims 1, 2, 4-10, and 12-15 will remain pending.

I. The Claimed Invention Is Not Obvious

Claims 1, 2, 4-10, and 12-15 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of Dualan et al., U18299 nucleotide sequence and abstract (hereinafter, the "Dualan reference"), Taylor et al., Drug Discovery Today, 1999, 4, 562-567 (hereinafter, the "Taylor reference"), U.S. Patent No. 5,801,154 (hereinafter, the "Baracchini reference"), Hayes et al., Mol. Cell. Biol., 1998, 18, 240-249 (hereinafter, the "Hayes reference"), and Krishnamoorthy et al., Biochem., 1997, 36, 960-969 (hereinafter, the "Krishnamoorthy reference"). Applicants traverse the rejection and respectfully request reconsideration because the claimed invention is not obvious in view of the combination of cited references.

The Dualan reference reports a nucleotide sequence that comprises 4193 nucleotides that encodes human damage-specific DNA binding protein DDBa p127 subunit (DDB1). The Dualan reference does not teach or suggest any compound targeted to such a sequence.

The Taylor reference reports general high-throughput approaches to target validation and gene function determination. The Taylor reference does not teach or suggest any compound targeted to damage-specific DNA binding protein 1, p127.

The Baracchini reference reports antisense oligonucleotide modulation of multidrug resistance-associated protein using a variety of chemically modified oligonucleotides. The Baracchini reference does not teach or suggest any compound targeted to damage-specific DNA binding protein 1, p127.

The Hayes reference reports that a putative DNA repair protein (DDB) can function as a transcription partner of transcription factor E2F1. The Hayes reference does not teach or suggest any compound targeted to damage-specific DNA binding protein 1, p127.

The Krishnamoorthy reference reports antibody inhibition of DDB as a means for testing the function of DDB. The Krishnamoorthy reference does not teach or suggest any compound targeted to damage-specific DNA binding protein 1, p127.

The Office Action mistakenly asserts that it would have been *prima facie* obvious for one skilled in the art to have used the cDNA sequence reported in the Dualan reference to make antisense sequences by the methods disclosed in the Taylor reference. The Office Action asserts that it would have also been obvious to chemically modify the antisense oligonucleotides as reported in the Baracchini reference. The motivation for making antisense oligonucleotides is allegedly found in the Hayes and Krishnamoorthy references.

The Office Action asserts that the Taylor reference teaches that "antisense-mediated inhibition of known sequences *in vitro* is routine to one of ordinary skill in the art" (Office Action, page 4). The Office Action also asserts that the Taylor reference teaches that "only 3-6 sequences need to be screened in order to find one that inhibits 66-95% *in vitro*" (Office Action, page 6). Thus, the Office Action appears to suggest that if a nucleotide sequence of a particular gene and methods of predicting oligonucleotides that can inhibit expression of the gene are generally known, then all oligonucleotides that inhibit expression of the gene are obvious. The Office Action asserts that the Taylor reference provides a reasonable expectation of success. This reasoning, however, is deficient.

The mere fact that the Taylor reference reports that antisense oligonucleotides that inhibit expression of a particular gene can be designed does not render all subsequent antisense oligonucleotide compounds obvious in view of a known gene sequence. Indeed, the Examiner's ultimate conclusion would require Applicants to either: 1) develop new methods of obtaining antisense oligonucleotides, in which case Applicants may be able to obtain product-by-process claims or method claims, or 2) develop antisense oligonucleotides to previously unknown gene sequences. In either case, all novel antisense oligonucleotides targeted to a known gene sequence would be deemed obvious in view of the current reasoning set forth in the Office Action. Rather than render the claimed invention obvious, the Taylor reference supports the enablement of antisense technology.

In addition, in evaluating obviousness, it is very clear that one must look to see if "the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art." *Dow Chemical*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Against this backdrop, the Federal Circuit has made it clear that it is improper to reject claims as "obvious to try" where the motivation to combine references arises merely because the subject matter of the claimed invention is a promising field for experimentation, although the prior art provides only general guidance as to particular form of the claimed invention or how to achieve it. *In re O'Farrell*, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988). The Taylor reference does not provide sufficient teachings that would have led one skilled in the art to do anything other than "try" unspecified methodology in predicting active antisense oligonucleotides. Indeed, in proper context, the Taylor reference reports:

> The best target sites are still determined empirically, although improvements in the potency of ONs and in the algorithms used for predicting accessible sites on the target mRNA have drastically reduced the number of oligonucleotides that must be screened to find one that is effective. Previous recommendations required the screening of 30-60 ONs per gene. Using high affinity chimeric oligomers and a bioinformatics program to select accessible sites, Woolf and coworkers have found that screening 3-6 oligomers per target is sufficient to find one that inhibits the gene with 66-95% efficiency (Sequitur, Natick, MA, USA) (unpublished data), significantly reducing the time and labor required to identify active ONs.

Thus, one skilled in the art examining the Taylor reference would not be able to determine: 1) what it is about the chimeric oligomers makes them chimeric (i.e., undisclosed chemical modifications), 2) what bioinformatics program should be used (i.e., undisclosed bioinformatics program, parameters, etc.), or 3) information for initial selection of accessible sites, based upon the disclosure in the Taylor reference. Further, the Taylor reference, rather than actually teaching one skilled in the art details sufficient to carry out such methods, simply refers to "unpublished data." Thus, the Taylor reference acts only as general guide (in the sense that it reports that active oligomers can generally be found) for screening oligomers and does not provide any details sufficient for one skilled in the art to carry out any particular methodology. See, *Chester v. Miller*, 906 F.2d 1574, 15 U.S.P.Q.2d 1333 (Fed. Cir. 1990) (reference must put subject matter at issue into possession of the public

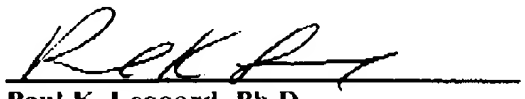
through an enabling disclosure). One skilled in the art having examined the entirety of the Taylor reference would, at most, conclude that it may be "obvious to try" to design compounds targeted to particular regions of a gene. Without more specific suggestions in the prior art, there is insufficient "expectation of success."

Thus, the claimed invention is not obvious in view of the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 665-6914 if there are any questions regarding Applicants' claimed invention. Please note that a Power of Attorney with Revocation and Change of Correspondence Address was filed September 18, 2003. Accordingly, please address all future correspondence to the practitioners at Customer Number 34138.

Respectfully submitted,



Paul K. Legaard, Ph.D.
Registration No. **38,534**

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COZEN O'CONNOR
1900 Market Street
Philadelphia, PA 19103-3508
Telephone: (215) 665-6914
Facsimile: (215) 701-2141

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